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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/699,716 08/27/96 HEATH

D 003/029/SAP

EXAMINER

18N2/1110

US ARMY MEDICAL RESEARCH &
MATERIAL COMMAND
ATTN MCMR JA JOHN MORAN
FORT DETRICK FREDERICK MD 21702-5012

CAPUTA, A

ART UNIT

PAPER NUMBER

1817

DATE MAILED:

11/10/97

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

See the attached.

Office Action Summary

Application No.
08/699,716

Applicant(s)
Heath et al.

Examiner
Anthony C. Caputa

Group Art Unit
1817

☒ Responsive to communication(s) filed on 11 Aug 1997

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-30 is/are pending in the application.

Of the above, claim(s) 18-29 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-17 and 30 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 5

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

Election/Restriction

1. Applicant's election of Group I, claims 1-17 in Paper No. 7 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
2. Claim 18-28 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention(s). Election was made **without** traverse in Paper No. 7.
3. Newly submitted claim 29 is directed to an invention that is independent or distinct from the invention originally claimed.

Since claim 29 is drawn to the protein, and the protein is distinct from the DNA of Group I for the reasons set forth in the Office Action mailed 7/11/97 (see page 3, first full paragraph) claim 29 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Applicants essentially argue in Paper No. 7, claim 29 should be linked with the DNA of Group I, since the protein is produced by a method that requires the DNA of Group I. Applicants are acknowledged. However, said argument is not sufficient to overcome the restriction requirement since the production of a product by a particular process does not impart novelty or unobviousness to a product when the product is taught by the prior art. See *In re Thorpe*, 227 USPQ 964 (CAFC 1985); *In re Marosi*, 218 USPQ 289, 292-293 (CAFC 1983); *In re Brown*, 173 USPQ 685 (CCPA 1972). Even if a particular process used to prepare a product is novel and unobvious over the prior art, the product per se, even when limited to the particular process, is unpatentable over the same product taught by the prior art.

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See In re King, 107 F. 2d 618, 620, 43 USPQ 400, 402 (CCPA 1939); In re Merz, 97 F. 2d 599, 601, 38 USPQ 143-45 (CCPA 1938); In re Bergy, 563 F. 2d 1031, 1035, 195 USPQ 344, 348 (CCPA 1977) vacated 438 US 902 (1978); and United States v. Ciba-Geigy Corp., 508 F. Supp. 1157, 1171, 211 USPQ 529, 543 (DNJ 1979).

Claim Objections

4. Claim 4 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 4 does not further claim 3 since SEQ ID NO. 1 as set forth in claim 3 inherently encodes for 521 amino acids as set forth in claim 3.

Claim Rejections - 35 USC § 112

5. Claims 1-17 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-17 and 30 are rejected for being vague and indefinite for use of the term "portion". As the claimed invention is drafted it is not clear what constitutes as a "portion"? Do applicants for instance intend one amino acid to constitute as a portion of the F1 (or V) antigen?

6. Claims 11 and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that pFIV and *E. coli* BRL are required to practice the claimed invention because claims 11 and 15 requires the use of said products. As a required element it must be

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known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of pFIV and *E. coli* BRL. See 37 CFR 1.802.

The specification does not provide a repeatable method for obtaining pFIV and *E. coli* BRL and it does not appear to be a readily available material. Since the specification does not provide the sequence and the precise structure of pFIV and *E. coli* BRL, the method of obtaining pFIV and *E. coli* BRL is not predictable and uncertain, and it would take undue experimentation to determine whether other constructs or *E. coli* would contain the same identifying characteristics as pFIV and *E. coli* BRL. Deposit of pFIV and *E. coli* BRL would satisfy the requirements of 35 U.S.C. § 112, first paragraph.

If a deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit has not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR §1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

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(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

© the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

In addition, a deposit of biological material that is capable of self-replication either directly or indirectly must be viable at the time of deposit and during the term of deposit. Viability may be tested by the depository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of a biological material not made under the Budapest Treaty must be filed in the application and must contain:

- 1) The name and address of the depository;
- 2) The name and address of the depositor;
- 3) The date of deposit;
- 4) The identity of the deposit and the accession number given by the depository;
- 5) The date of the viability test;
- 6) The procedures used to obtain a sample if the test is not done by the depository; and
- 7) A statement that the deposit is capable of reproduction.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the construct pFIV and/or *E. coli* BRL described in the specification as filed is the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the

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biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundack, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR §1.801-1.809 for further information concerning deposit practice.

7. Claims 1-10, 12-17, and 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabled in how to make and use an isolated DNA as claimed. The specification is non-enabled for DNA encoding, mutants (deletions or substitutions), chemical modifications, truncations of SEQ ID No: 1 (or 2) which are encompassed in the claims.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (see Burgess et al.). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduce the biological activity of the mitogen (see Lazar et al.). These references demonstrate that a even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein. In view of the lack of guidance, lack of examples, and lack of predictability associated with regard to producing and using the myriad or derivatives encompassed in the scope of the claims one skilled in the art would be forced into undue experimentation in order to practice broadly the claimed invention.

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8. Claims 1-10, 12-17, and 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses of a FI-V DNA fragment comprising SEQ ID NO:1 which has the particular amino acid sequence of SEQ ID NO:2. This DNA meet the written description and enablement provisions of 35 U.S.C. 112, first paragraph. However, the claims are directed to broadly encompass DNA of other sequences, which correspond to mutated sequences, allelic variants, splice variants, sequences that have similarity or homology, and so forth. None of the these DNA meet the written description provision of 35 USC 112, first paragraph.

Vas-Cath Inc. V. Makurhar, 19 USPQ2d 1111, makes clear that applicant must convey with reasonable clarity to those skilled in the art, as the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry whatever is now claimed (see page 1117). The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed. (See Vas-Cath Inc. V. Makurhar, page 1116.).

With the exception of FI-V DNA fragment comprising SEQ ID NO:1 which has the particular amino acid sequence of SEQ ID NO:2 the skilled artisan can not envision the detailed chemical structure of the encompassed DNA and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that is part of the invention and reference to a potential method for isolating it, The nucleic acid itself is required,. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.* 18 USPQ 2d 1016.

One can not describe what one has not conceived. See Fiddes v. Baird 30 USPQ 2d 1481, 1483.

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Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Price et al. (J. Bacteriology 171(10):5646-53 10/89).

Price et al disclose a an isolated DNA which comprises a sequence which contains the sequence ATG....TGA. Since the DNA has a portion of the F1 capsular antigen (e.g. ATG) and a portion of the V antigen and the sequence is at least 30 nucleotides the claimed invention is anticipated over the disclosure by Price et al.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. Claims 1-17, and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/18231 (Titball et al.-31) and further in view of: WO 95/24475 (Titball et al.-'75); or Leary et al. Infection and Immunity 63(8): 2854-58 8/95, publicly available as of 7/25/97).

Titball et al.-31' teaches the gene encoding the F1 antigen has been cloned and sequenced. Titball et al.-31 teaches using DNA recombinant constructs are capable of expressing a protein which produces a protective immune response (see pages 2-5). Titball et al.-31 discloses vectors

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(i.e. plasmids) that are capable of transforming a human or animal gut colonizing microorganism such that it is capable of expressing a protein which produces a protective immune response against *Yersina pestis*. Titball et al.-31 discloses using a pharmaceutically acceptable carrier in the vaccine composition. Titball et al.-31 discloses of using such host cells as *Salmonella* and *E. coli* to express the protein (see Example 4). Titball et al.-31 discloses of a F1 protein (see SEQ ID No. 10) which has the same amino acid sequence as the F1 Protein. Titball et al.-31 discloses of using recombinant DNA encoding fusion proteins of the F1 protein (See page 5). Titball does not teach of a DNA that encodes a F1 protein fused to the V protein as recited.

Leary et al teach of a DNA expression vector that expresses a V antigen (see abstract). Leary et al.. teach that the V antigen protect mice against the plague (see abstract). While Titball et al.-31 does not teach of a DNA that encodes a F1 protein fused to the V protein it would have been obvious to one of ordinary skill in the art to link the gene encoding the F1 protein as set forth by Titball et al. 31 to the gene encoding the V antigen as set forth by Leary et al since a DNA construct encoding the fusion protein would have been expected to provide a vaccine with higher efficacy than a DNA construct which only encodes for the V antigen (or F1 antigen). Furthermore, it would have been obvious for one of ordinary skill in the art to link the gene encoding the F1 protein to the gene encoding the V protein since the time and cost to make a F1 antigen fused to the V antigen would have been expected to be less than making the antigens independently. Leary et al does not characterize the gene encoding the V antigen as having the sequence of the V antigen as recited (i.e. SEQ ID NOS 1 or 2). Nevertheless it would have been expected that they are the same or an obvious or analogous variant since they have the same properties (both encode for a V antigen which is protective).

Titball et al-75 teach of a DNA constructs that expresses a V antigen (see abstract). Titball et al-75 teach that the V antigen can be used as a vaccine (see abstract). Titball et al-75 teaches of the sequence of the gene encoding the V antigen. While Titball et al.-31 does not teach of a DNA that encodes a F1 protein fused to the V protein it would have been obvious to one of

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ordinary skill in the art to link the gene encoding the F1 protein as set forth by Titball et al. 31 to the gene encoding the V antigen as set forth by Titball et al -75 since a DNA construct encoding the fusion protein would have been expected to provide a vaccine with higher efficacy than a DNA construct which only encodes for the V antigen (or F1 antigen). Furthermore, it would have been obvious for one of ordinary skill in the art to link the gene encoding the F1 protein to the V protein since the time and cost to make a F1 antigen fused to the V antigen would have been expected to be less than making the antigens independently.

Titball et al-75 does not characterize the gene encoding the V antigen as having the sequence of the V antigen as recited (i.e. SEQ ID NOS 1 or 2). Nevertheless it would have been expected that they are obvious or analogous variant since they have the same properties (both encode for a V antigen which is protective).

Titball et al. 31 does not teach of using virus as a host nor a eukaryotic vector as recited. Nevertheless, since using a virus as a host and a eukaryotic vector as a vector were well known in the art at the time of the invention one of ordinary skill in the art at the time of the invention would have been motivated and expected to use a virus or eukaryotic vector to express the F1-V antigen.

Titball et al. 31 does not teach of using the pFIV as a construct which has a EcoR1 site linking the gene encoding the F antigen to the V antigen. Titball-31 does not teach using the *E coli* strain BLR as a host cell. However, since the starting materials pET 19b and *E coli* strain BLR were available from Novagen, and a synthetic linker having the restriction site EcoR1 at the time of invention was known to ligate two pieces of DNA, the claimed invention is rendered obvious over the prior art.

Titball et al. 31 does not teach of fusing the F1 antigen at its carboxyl terminal end to the amino terminal end of the V antigen. Nevertheless since it would have been expected that one of ordinary skill in the art would have fused the F1 antigen to the V antigen either at its carboxyl terminal end or the N-terminal end the claimed invention is rendered obvious.


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13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Anthony C. Caputa, whose telephone number is (703)-308-3995. The examiner can be reached on Monday-Thursday from 8:30 AM-6:00 PM. The examiner can be reached on alternate Fridays. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703)-308-0196.

Papers related to this application may be submitted to Art Unit 1817 by facsimile transmission. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The Fax number is (703)-308-4242.

Anthony C. Caputa, Ph.D.

November 8, 1997



**ANTHONY C. CAPUTA
PRIMARY EXAMINER
GROUP 1800**